REMARKS

The Office Action dated May 5, 2008 has been received and carefully studied.

The Examiner maintains the rejection of claim 8 under 35 U.S.C. §103(a) as being unpatentable over Santo et al., JP 2000-211239. The Examiner relies on the case of *Pfizer, Inc. v. Apotex, Inc.*, 82 U.S.P.Q.2d 1321 (Fed. Cir. 2007) in support of the rejection.

The rejection is respectfully traversed.

In the *Pfizer* case, the Court found that the besylate salt of amlodipine was obvious in view of a primary reference which generically disclosed pharmaceutically acceptable salts of amlodipine, and secondary references which disclosed that besylate salts were FDA approved pharmaceutically-acceptable salts, and that showed the aryl sulphonic acids, including benzene sulphonic acid, exhibit excellent properties including solubility and stability.

The Examiner states that the Court in *Pfizer* rejected the notion that unpredictability could be equated with nonobviousness because there were only a finite number (53) of pharmaceutically acceptable salts to be tested for improved properties. However, Applicants respectfully but vigorously submit that the Examiner's characterization of the holding in the *Pfizer* case is incorrect. The Court in *Pfizer* expressly stated that the outcome of the case need not rest heavily on the size of the genus of pharmaceutically-acceptable anions disclosed by the secondary reference, because out of the list of 53 anions, one of ordinary

skill in the art would have favorably considered benzene sulphonate, because of its known acid strength, solubility and other known chemical characteristics as reported in several other publications Pfizer admitted as being prior art. Importantly, the Court stated that these other publications provided ample motivation to narrow the genus of 53 pharmaceutically-acceptable anions to just a few, including benzene sulphonate. **This further narrowing of the genus of 53 anions down to just a few anions in view of the teachings of the prior art was critical to the Court's decision:**

> "[W]e hold that the optimization of the acid addition salt formulation for an active pharmaceutical ingredient would have been obvious where as here the acid addition salt formulation has no effect on the therapeutic effectiveness of the active ingredient and the prior art heavily suggests the particular anion used to form that salt." (Emphasis added.)

That is, the prior art in *Pfizer* taught that aryl sulphonic acids, such as benzene sulphonic acids, considerably increase the solubility of pharmaceuticals containing one or more basically reacting nitrogen atoms, specifically identified besylate as the preferred pharmaceutically-acceptable acid addition salt form of a pharmaceutical compound, disclosed an intermediate dihydropyridine compound useful in the form of an acid addition salt derived from benzene sulphonate, and disclosed the besylate acid addition salt form of a pharmaceutical composition having excellent pharmacokinetic properties, near-optimal solubility, and improved stability. As stated by the *Pfizer* Court:

> "Taken together, these references provide ample motivation to narrow the genus of 53 pharmaceutically-acceptable anions disclosed by Berge to a few, including benzene sulphonate."

This is consistent with the case of *In re Baird*, 29 U.S.P.Q.2d 1550 (Fed. Cir. 1994), where the Court also looked for some suggestion in the prior art that would lead to choosing one of many alternatives set forth in the disclosure of a genus:

> "Given the vast number of diphenols encompassed by the generic diphenol formula in Knapp, and the fact that the diphenols that Knapp specifically discloses to be 'typical', 'preferred', and 'optimum' are different from and more complex than bisphenol A, we conclude that Knapp does not teach or fairly suggest the selection of bisphenol A." (29 U.S.P.Q.2d at 1552).

The application of the same standard articulated in the *Pfizer* case was applied by the Court in *Baird*, but the outcome was different in *Baird* because there was nothing in the prior art that guided the skilled artisan to choose one of many alternatives. See also *In re Bell*, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993).

The same "narrowing of the genus" suggested by the prior art that was present in *Pfizer* is not present in the instant case; the prior art does not suggest a narrowing of the 36 different possible anions in the present case to the one recited in claim 8. Indeed, the Sugimachi et al. reference actually expresses preference for other anions, not the CF_3SO_3 anion claimed, and these preferences are consistent with anions disclosed in the Santo primary reference. As previously argued by Applicant, since R_1-R_8 in the generic Formula [II] of Santo et al. can independently

be an alkynyl group, an alkenyl radical, an alkyl group, an alkoxyalkyl group or an aralkyl radical, when these substituents are considered in combination with the 36 different possible anions, a very large number of compounds are encompassed by the generic Formula [II]. This is consistent with the facts of the *Baird* case. The prior art does not provide any direction to choose the particular R_1-R_8 groups and the particular anion recited in the instant claim 8. In this context, Tables 9-12 of Santo show 38 specific compounds of the Formula [II]. Among these, only five compounds, namely, Formulas [II]-4, [II]-16, [II]-17, [II]-19 and [II]-25, are compounds wherein R_1-R_8 are branched or straight chain butyl or pentyl groups as required by the instant claim 8. The anions of these compounds are Br, SbF_6, ClO_4 and NO_3. Accordingly, these specific disclosures of species within the genus of Formula [II] in Santo do not motivate or in any way "fairly suggest" the selection of CF_3SO_3 as the anion when the proper alkyl groups are chosen. There is nothing else in the disclosure of Santo that motivates the selection of the particular R groups and the CF_3SO_3 anion to arrive at the compounds of claim 8. Importantly, Sugimachi et al. expressly discloses a preference for the anion in the diimmonium compound as BF_4^-, PF_6^-, ClO_4^- or SbF_6^- (see paragraph [0048]).

In addition, the Examiner's dismissal of the unexpected results set forth in the Toriniwa Declaration "in view of the Court decision" is erroneous. The Court decision in *Pfizer* found that a *prima facie* case of obviousness had been established, it did not simply dismiss the evidence of unexpected results that

were of record. Indeed, the *Pfizer* Court went on to evaluate the evidence of unexpected results present in that case, and determined that since evidence of what should be expected was not of record, the unexpected results could not be probably evaluated.

In the unlikely event the Examiner maintains the position that a *prima facie* case of obviousness has been established, proper consideration of the evidence of record is mandated, and is respectfully requested.

In summary, it was critical to the outcome of the *Pfizer* case that the secondary references suggested the particular salt being claimed, thereby significantly narrowing the genus. Such a suggestion did not exist in *Baird*, and does not exist in the present case. In fact, the prior art suggests a direction away from the particular anion claimed. Furthermore, the Examiner's dismissal of the evidence of unexpected results "in view of the Court decision" in *Pfizer* is erroneous.

Applicants respectfully submit that no *prima facie* case of obviousness has been established, and the claimed compounds exhibit unexpected results.

Reconsideration and allowance are respectfully requested in view of the foregoing.

Respectfully submitted,

Kevin S. Lemack
Reg. No. 32,579
176 E. Main Street - Suite 5
Westboro, Massachusetts 01581
TEL: (508) 898-1818